IN THE CLAIMS

Please amend claims 17, 32-38, and 44, as shown below. Please add new claims 55-74. The following listing of claims replaces all prior listings.

1-16. (Canceled).

17. (Currently amended) A method for analyzing a plurality of proteomic mixtures, said method comprising differentiating the mixtures on the basis of activity, said differentiating comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct; and

(b) determining the presence of said adduct in each of said mixtures;

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site.

18-31. (Canceled)

32. (Currently amended) A method according to Claim ~~17 or~~ 53, additionally comprising characterizing said active target members conjugated with said probe(s).

33. (Currently amended) A method according to Claim 32, wherein said characterizing comprises degrading said active target members and determining the resulting fractions by mass spectrometry.

34. (Currently amended) A method according to Claim ~~17 or~~ 53, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

35. (Currently amended) A method according to Claim ~~17 or~~ 53, wherein said activity-based probe(s) comprises a detectable label.

36. (Currently amended) A method according to Claim ~~17 or~~ 53, wherein said proteomic mixture is in an intact cell.

37. (Currently amended) A method according to Claim ~~17 or~~ 53, further comprising analyzing for the presence of proteins conjugated with said probe(s) using simultaneous individual capillary electrokinetic analysis or capillary HPLC.

38. (Currently amended) A method ~~according to claim 17~~ for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct; and

(b) determining the presence of said adduct in each of said mixtures;

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site, wherein said activity-based probe(s) are of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L.

39. (Previously presented) A method according to Claim 38, wherein F is a sulphonyl group and R is other than H and bonded to F.

40. (Previously presented) A method according to Claim 38, wherein F is a fluorophosphonyl or fluorophosphoryl group.

41. (Canceled).

42. (Previously presented) A method according to any of Claims 32, 33, 35-38, or 40, wherein said activity-based probe(s) are fluorophosphonate-biotin (FP-biotin).

43. (Previously presented) A method according to any of Claims 32, 33, 35-38, or 40, wherein said activity-based probe(s) are FP-peg-biotin.

44. (Currently amended) A method according to any of Claims ~~32, 33, 35-39~~ 38, 39, or 53 wherein said activity-based probe(s) are selected from the group consisting of 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

45. (Previously presented) A method according to claim 44 wherein said activity-based probe is 1-(2-pyridylsulfonyl)oxo-octane.

46. (Previously presented) A method according to Claim 34 wherein said activity-based probe(s) are selected from the group consisting of FP-biotin, FP-peg-biotin, 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-

biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

47-52. (Canceled).

53. (Previously presented) A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

combining each of said proteomic mixtures with at least one activity-based probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe(s) to said target members;

determining the presence of target members conjugated with said probe in each of said proteomic mixtures;

whereby the presence of said target members conjugated to said probe(s) in said proteomic mixtures is indicative of the presence of active target members in said mixtures,

wherein said activity-based probe(s) have the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L.

54. (Withdrawn) A method for screening for the bioactivity of a candidate compound toward a group of related target proteins in a proteomic mixture of proteins from a cell, employing at least one probe, each probe characterized by comprising a reactive functionality group specific for said group of target proteins and a ligand and said probe, said method comprising:

(a) combining at least one probe with an untreated portion of said mixture and with a portion inactivated with a non-covalent agent under conditions for reaction with said target proteins;

(b) sequestering proteins conjugated with said at least one probe from each of said mixtures;

(c) determining the proteins that are sequestered; and

(d) comparing the amount of each of the proteins sequestered from the untreated portion and the inactivated portion as indicative of the bioactivity of said candidate compound with said target proteins.

55. (New) A method according to Claim 17, additionally comprising characterizing said active target members conjugated with said probe(s).

56. (New) A method according to Claim 55, wherein said characterizing comprises degrading said active target members and determining the resulting fractions by mass spectrometry.

57. (New) A method according to Claim 17, employing a plurality of activity-based probes having different reactive functionalities specific for different groups of related proteins.

58. (New) A method according to Claim 17, wherein said activity-based probe(s) comprises a detectable label.

59. (New) A method according to Claim 17, wherein said proteomic mixture is in an intact cell.

60.(New) A method according to Claim 17, further comprising analyzing for the presence of proteins conjugated with said probe(s) using simultaneous individual capillary electrophoretic analysis or capillary HPLC.

61. (New) A method according to Claim 17, wherein said activity-based probe(s) are of the formula:

R* (F – L) -X

wherein:

X is a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality to add a ligand;

L is a linking group;

F is a functional group reactive at an active site of a target enzyme; and

R is H or a moiety of less than 1kDal providing specific affinity for said target enzymes;

the * intends that R is a part of F or L.

62. (New) A method according to Claim 61, wherein F is a sulphonyl group and R is other than H and bonded to F.

63. (New) A method according to Claim 61, wherein F is a fluorophosphonyl or fluorophosphoryl group.

64. (New) A method according to any of Claims 55, 56, 58-61, or 63, wherein said activity-based probe(s) are fluorophosphonate-biotin (FP-biotin).

65. (New) A method according to any of Claims 55, 56, 58-61, or 63, wherein said activity-based probe(s) are FP-peg-biotin.

66. (New) A method according to any of Claims 55, 56, or 58-62, wherein said activity-based probe(s) are selected from the group consisting of 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

67. (New) A method according to claim 66, wherein said activity-based probe is 1-(2-pyridylsulfonyl)oxo-octane.

68. (New) A method according to Claim 57, wherein said activity-based probe(s) are selected from the group consisting of FP-biotin, FP-peg-biotin, 10-((2-pyridylsulfonyl)oxo)-N-biotinamidopentyldecanamide, 10-((Benzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((*p*-Toluenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Methoxybenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Methylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((Butylsulfonyl)oxo)-*N*-biontinamidopentyldecanamide, 10-((Octylsulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((4-Nitrobenzenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((8-Quinolinesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Naphthalenesulfonyl)oxo)-*N*-biotinamidopentyldecanamide, 10-((2-Thiophenesulfony)oxo)-*N*-biotinamidopentyl)decanamide, α-undecylenyl alcohol, ((2-pyridylsulfonyl)oxo)-10-undecene, 10-((2-pyridylsulfonyl)oxo)-decanoic acid, 1-(2-pyridylsulfonyl)oxo-octane, 1-(2-pyridylsulfonyl)oxo-ethane, and 1-(methanesulfonyl)oxo-octane.

69. (New) A method for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct;

(b) determining the presence of said adduct in each of said mixtures,

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site; and

(c) characterizing said active target members conjugated with said probe(s).

70. (New) A method according to Claim 69, wherein said characterizing comprises degrading said active target members and determining the resulting fractions by mass spectrometry.

71. (Currently amended) A method for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with a plurality of activity-based probes, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probes include a functionality allowing conjugation of said probes to said target members,

whereby said probes are conjugated to said target members, under conditions for conjugation of said probes to said target members to form an adduct;

(b) determining the presence of said adduct in each of said mixtures,

wherein the plurality of activity-based probes has different reactive functionalities specific for different groups of related proteins,

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site.

72. (New) A method for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct;

(b) determining the presence of said adduct in each of said mixtures,

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site, and wherein said activity-based probe(s) comprises a detectable label.

73. (New) A method for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct;

(b) determining the presence of said adduct in each of said mixtures,

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site, wherein said proteomic mixture is in an intact cell.

74. (New) A method for analyzing a plurality of proteomic mixtures, said method comprising:

(a) combining each of said mixtures with at least one activity-based probe, wherein:

(a1) each mixture includes a group of related proteins, the group comprising active target members;

(a2) said probe(s) includes a functionality allowing conjugation of said probe to said target members,

whereby said probe(s) is conjugated to said target members, under conditions for conjugation of said probe(s) to said target members to form an adduct;

(b) determining the presence of said adduct in each of said mixtures,

whereby the presence of said adduct in said mixtures is indicative of the presence of active target members in said mixtures, wherein said related proteins include a common functionality for conjugation at an active site;

the method further comprising analyzing for the presence of proteins conjugated with said probe(s) using simultaneous individual capillary electrophoretic analysis or capillary HPLC.